

## **Commentary to habilitation thesis**

Despite of advances in the diagnosis and treatment of epilepsy remain approximately 30%-40% of the patients pharmaco-resistant. The International League Against Epilepsy (ILAE) defines drug-resistant epilepsy as “failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom”. Only parts of these patients can be offered curative epileptosurgical solutions or other non-pharmacological treatment options (vagus nerve stimulation, ketogenic diet, etc.).

The pharmaco-resistance to antiseizure drugs (ASD) per se is not a possible therapeutic target, as ASDs themselves do not prevent the development of epilepsy, merely blocking the seizures as they arise. Moreover, there is no evidence that they influence the course of epilepsy. There are no clinical tools or guidelines for predicting therapeutic response in individual patients, leaving them no choice other than to try all antiseizure drugs available as they suffer debilitating seizures with no relief.

Current therapy is limited to suppressing the symptoms of the disease- epileptic seizures, and does not allow the elimination of the cause (except epileptosurgery) or its prevention during the process of epileptogenesis (in the patients who are at risk due to genetic predisposition or after brain insult).

The aim of research in the epileptology is discovery of the drugs that would not only suppress seizures, but ideally work as medication which prevent or modify the process of epileptogenesis, the medication working as disease-modifying drugs (DMD) and the treatment due to progressive process of neurodegeneration, neuroinflammation and neuronal hyperexcitability leading to the development of pharmaco-resistance in epilepsy.

The discovery of predictive biomarkers and early identification of pharmaco-resistant patients and patients who are at the risk of development of epilepsy (biomarkers of epileptogenesis) is the highest priority of current epileptology research.

This habilitation thesis is conceived as a collection of 6 articles previously published by the author and her colleagues. It contains individual chapters dealing with the basic aspects of epileptogenesis and pharmaco-resistance in epilepsy. Each chapter is followed by commentaries introducing the topic of each publication, describing the current state of knowledge and how the author has contributed to knowledge in this field. The work is based

on research activities at the authors' workplaces, the Department of Paediatric Neurology, University Hospital Brno; the Faculty of Medicine, Masaryk University; and Central European Institute of Technology.

In the future, new therapeutic procedures should offer a wide range of options, respecting the specifics of individual forms of epilepsy as well as individual differences between patients with regard to the development and prognosis of the disease.

### Annex 1

**AULICKA, S.**, K. CESKA, J. SANA, T. LOJA, P. JABANDZIEV, J. PAPEZ, P. DANHOFER, H. VINOHRADSKA, I. DOLEZALOVA, M. BRAZDIL, P. STOURAC, H. OSLEJSKOVA a O. SLABY. The role of inflammation in etiopathogenesis of pharmacoresistant epilepsy and refractory status epilepticus. *Ceska a Slovenska Neurologie a Neurochirurgie* [online]. 2020, **83**(1), 8–13. ISSN 1210-7859. Dostupné z: doi:[10.14735/amcsnn20208](https://doi.org/10.14735/amcsnn20208)

Experimental work	Supervision	Manuscript	Research direction
30%	-	70%	30%

### Annex 2

BOHOSOVA, Julia, Jiri VAJCNER, Petr JABANDZIEV, Hana OSLEJSKOVA, Ondrej SLABY a **Stefania AULICKA** *\*(corresponding author)\**. MicroRNAs in the development of resistance to antiseizure drugs and their potential as biomarkers in pharmacoresistant epilepsy. *Epilepsia* [online]. 2021, **62**(11), 2573–2588. ISSN 0013-9580. Dostupné z: doi:[10.1111/epi.17063](https://doi.org/10.1111/epi.17063)

Experimental work	Supervision	Manuscript	Research direction
-	70%	30%	30%

### Annex 3

CESKA, Katarina, **Stefania AULICKA** *\*(corresponding author)\**, Ondrej HORAK, Pavlina DANHOFER, Pavel RIHA, Radek MARECEK, Jan SENKYRIK, Ivan REKTOR, Milan BRAZDIL a Hana OSLEJSKOVA. Autosomal dominant temporal lobe epilepsy associated with heterozygous reelin mutation: 3 T brain MRI study with advanced neuroimaging methods. *Epilepsy & Behavior Case Reports* [online]. 2019, **11**, 39–42. ISSN 2213-3232. Dostupné z: doi:[10.1016/j.ebcr.2018.10.003](https://doi.org/10.1016/j.ebcr.2018.10.003)

Experimental work	Supervision	Manuscript	Research direction
20%	60%	50%	30%

### Annex 4

SCHILLING, Kurt G., Francois RHEAULT, Laurent PETIT, Colin B. HANSEN, Vishwesh NATH, Fang-Cheng YEH, Gabriel GIRARD, Muhamed BARAKOVIC, Jonathan RAFAEL-PATINO, Thomas YU, Elda FISCHI-GOMEZ, Marco PIZZOLATO, Mario OCAMPO-PINEDA, Simona SCHIAVI, Erick J. CANALES-RODRIGUEZ, Alessandro DADUCCI, Cristina

GRANZIERA, Giorgio INNOCENTI, Jean-Philippe THIRAN, Laura MANCINI, Stephen WASTLING, Sirio COCOZZA, Maria PETRACCA, Giuseppe PONTILLO, Matteo MANCINI, Sjoerd B. VOS, Vejay N. VAKHARIA, John S. DUNCAN, Helena MELERO, Lidia MANZANEDO, Emilio SANZ-MORALES, Angel PENA-MELIAN, Fernando CALAMANTE, Arnaud ATTYE, Ryan P. CABEEN, Laura KOROBOVA, Arthur W. TOGA, Anupa Ambili VIJAYAKUMARI, Drew PARKER, Ragini VERMA, Ahmed RADWAN, Stefan SUNAERT, Louise EMSELL, Alberto DE LUCA, Alexander LEEMANS, Claude J. BAJADA, Hamied HAROON, Hojjatollah AZADBAKHT, Maxime CHAMBERLAND, Sila GENC, Chantal M. W. TAX, Ping-Hong YEH, Rujirutana SRIKANCHANA, Colin D. MCKNIGHT, Joseph Yuan-Mou YANG, Jian CHEN, Claire E. KELLY, Chun-Hung YEH, Jerome COCHEREAU, Jerome J. MALLER, Thomas WELTON, Fabien ALMAIRAC, Kiran K. SEUNARINE, Chris A. CLARK, Fan ZHANG, Nikos MAKRIS, Alexandra GOLBY, Yogesh RATHI, Lauren J. O'DONNELL, Yihao XIA, Dogu Baran AYDOGAN, Yonggang SHI, Francisco Guerreiro FERNANDES, Mathijs RAEMAEKERS, Shaun WARRINGTON, Stijn MICHIELSE, Alonso RAMIREZ-MANZANARES, Luis CONCHA, Ramon ARANDA, Mariano Rivera MERAZ, Garikoitz LERMA-USABIAGA, Lucas ROITMAN, Lucius S. FEKONJA, Navona CALARCO, Michael JOSEPH, Hajer NAKUA, Aristotle N. VOINESKOS, Philippe KARAN, Gabrielle GRENIER, Jon Haitz LEGARRETA, Nagesh ADLURU, Veena A. NAIR, Vivek PRABHAKARAN, Andrew L. ALEXANDER, Koji KAMAGATA, Yuya SAITO, Wataru UCHIDA, Christina ANDICA, Masahiro ABE, Roza G. BAYRAK, Claudia A. M. Gandini WHEELER-KINGSHOTT, Egidio D'ANGELO, Fulvia PALESI, Giovanni SAVINI, Nicolo ROLANDI, Pamela GUEVARA, Josselin HOUENOU, Narciso LOPEZ-LOPEZ, Jean-Francois MANGIN, Cyril POUPON, Claudio ROMAN, Andrea VAZQUEZ, Chiara MAFFEI, Mavilde ARANTES, Jose Paulo ANDRADE, Susana Maria SILVA, Vince D. CALHOUN, Eduardo CAVERZASI, Simone SACCO, Michael LAURICELLA, Franco PESTILLI, Daniel BULLOCK, Yang ZHAN, Edith BRIGNONI-PEREZ, Catherine LEBEL, Jess E. REYNOLDS, Igor NESTRASIL, Rene LABOUNEK, Christophe LENGLET, Amy PAULSON, **Stefania AULICKA**, Sarah R. HEILBRONNER, Katja HEUER, Bramsh Qamar CHANDIO, Javier GUAJE, Wei TANG, Eleftherios GARYFALLIDIS, Rajikha RAJA, Adam W. ANDERSON, Bennett A. LANDMAN a Maxime DESCOTEAUX. Tractography dissection variability: What happens when 42 groups dissect 14 white matter bundles on the same dataset? *Neuroimage* [online]. 2021, **243**, 118502. ISSN 1053-8119. Dostupné z: doi:[10.1016/j.neuroimage.2021.118502](https://doi.org/10.1016/j.neuroimage.2021.118502)

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Experimental work	Supervision	Manuscript	Research direction
30%	10%	30%	30%

## Annex 5

**RUSNAKOVA, Stefania**, Pavel DANIEL, Jan CHLADEK, P. JURAK a Ivan REKTOR. The Executive Functions in Frontal and Temporal Lobes: A Flanker Task Intracerebral Recording Study. *Journal of Clinical Neurophysiology* [online]. 2011, **28**(1), 30–35. ISSN 0736-0258. Dostupné z: doi:[10.1097/WNP.0b013e31820512d4](https://doi.org/10.1097/WNP.0b013e31820512d4)

Experimental work	Supervision	Manuscript	Research direction
50%	-	80%	30%

## Annex 6

**AULICKA, Stefania Rusnakova**, Pavel JURAK, Jan CHLADEK, Pavel DANIEL, Josef HALAMEK, Marek BALAZ, Martina BOCKOVA, Jan CHRASTINA a Ivan REKTOR.

Subthalamic nucleus involvement in executive functions with increased cognitive load: a subthalamic nucleus and anterior cingulate cortex depth recording study. *Journal of Neural Transmission* [online]. 2014, **121**(10), 1287–1296. ISSN 0300-9564. Dostupné

z: doi:[10.1007/s00702-014-1191-5](https://doi.org/10.1007/s00702-014-1191-5)

<b>Experimental work</b>	<b>Supervision</b>	<b>Manuscript</b>	<b>Research direction</b>
50%	-	80%	30%